

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF APPEALS AND INTERFERENCES**

Application of: Rein *et al.*

Confirmation No.: 8812

Serial No.: 09/980,727

Group Art Unit: 1618

Filed: July 8, 2002

Examiner: Rogers, James William

For: METHOD FOR PRODUCING A WATER-
INSOLUBLE AMORPHOUS OR PARTIALLY
AMORPHOUS CONTROLLED-RELEASE MATRIX

Attorney Docket No.: 11390-009

REPLY BRIEF

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REPLY BRIEF UNDER 37 C.F.R. § 41.41

Mail Stop Reply Brief-Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In response to the Examiner's Answer mailed January 11, 2011, and in accordance with 37 C.F.R. § 41.41, Appellants respectfully submit this Reply Brief and request consideration of the remarks made herein. Appellants' Brief on Appeal was filed on October 29, 2010. The filing of this Reply Brief is considered timely since it is being filed within two months of the mailing of the Examiner's Answer.

It is estimated that no fee is required for filing this Reply Brief. However, should the Patent and Trademark Office determine otherwise, please charge the necessary fee to Jones Day Deposit Account No. 50-3013.

This Reply Brief is accompanied by a Request for Oral Hearing and the associated fee required by 37 C.F.R. § 41.20(b)(3).

REPLY TO THE EXAMINER'S ANSWER

Appellants respectfully maintain the arguments as set forth in the Brief on Appeal (hereinafter the "Appeal Brief") which was filed on October 29, 2010, and which is hereby incorporated by reference in its entirety. Furthermore, Appellants respectfully submit the following arguments in response to the Examiner's Answer (hereinafter "the Examiner's Answer" or the "Answer") to the Appeal Brief.

I. The Examiner's Response to Appellants' Arguments That Claims 10, 16-18 and 23-32 Are Not Anticipated Is Erroneous

A. With respect to the rejection of claims 10, 16-18 and 23-32 as anticipated by European Patent Publication No. 0 580 860A1 to Nakamichi *et al.* ("Nakamichi"), Appellants respectfully submit that the response in the Examiner's Answer to Appellants' arguments is erroneous.

According to the Examiner, Nakamichi teaches a method of manufacturing a pharmaceutical solid dispersion, produced without heating chemicals and polymeric carriers above their respective melting points. Thus, according to the Examiner, Nakamichi discloses the same processing technique and the product containing the same materials processed from such method. However, the Examiner fails to take into account that the solid dispersions of Nakamichi are not controlled released dispersions and are not vitrified, which is each required by the pending claims. The Examiner fails to appreciate the specific teaching of Nakamichi on page 6, lines 39-48, which teaches that their dosage forms are not controlled release dosage forms:

In October 1991, a technology for the manufacture of a controlled release dosage form utilizing a single-screw extruder was disclosed . . .

However, the technology disclosed in the above literature is a process using a single-screw extruder which is by far inferior to the twin-screw extruder as pointed out hereinbefore and the product is also *distinct* from the solid dispersion provided by the process of the present invention. Furthermore, the above technology is intended for the manufacture of a slow [controlled] release dosage form and this slow release dosage form is manufactured at high temperature.

Therefore, the above technology is irrelevant to the process of the invention which is intended for the manufacture of a solid

dispersion overcoming the disadvantages of the prior art fusion and solvent processes (emphasis added).

Thus, the dosage forms taught by Nakamichi are distinct from claimed controlled release dosage forms. In view of this teaching alone, Nakamichi cannot anticipate the claimed method or products.

In view of the foregoing, and Appellants' previously submitted remarks, Appellants submit that this rejection should be reversed and that the claimed method for producing controlled release matrices and the controlled release matrices set forth in claims 10, 16-18 and 23-32 are not anticipated by Nakamichi.

B. With respect to the rejection of claims 10, 17-18 and 23-32 as anticipated by International Patent Publication No. WO 92/15285 to Lentz *et al.* ("Lentz"), Appellants respectfully submit that the response in the Examiner's Answer to Appellants' arguments is erroneous.

With regard to the Examiner's assertion that Lentz clearly teaches that the active ingredient may be added to the starch prior to destructureization, Appellants point out that whether the starch is first destructureized and then admixed with an active ingredient, or mixed with an active ingredient, and then submitted to a destructureization process (see Lentz at page 17, line 34 to page 18, line 1), in either case the starch is nevertheless destructureized, and thus, different from the claimed compositions. As explained previously, the molecularly dispersed starch of Lentz is soft and rubbery and, thus, subjected to above the glass transition temperature. Appellants invite the Examiner's attention to page 12, lines 5-25 of Lentz, which discusses that the formation of molecularly dispersed starch (MDS) requires that the starch being melted above its glass transition temperature.

Further, Appellants direct the Board's attention to the submitted experimental evidence comparing the process of the present invention, where the temperature of the extruder orifice is below 100°C, with the process taught by Lentz, where the temperature of the extruder orifice is above 100°C, e.g., 120°C or up to 240°C. The Board's attention is invited to the Rein Declaration at Paragraphs 8 to 12, which was submitted originally with the Reply under 37 C.F.R. § 1.111 on February 12, 2007. In the Declaration, Dr. Rein sets forth experiments that were performed or supervised and directed by him, and their results demonstrating that using the process of Lentz (at or over 100°C) only popped (foamed) products are produced, whereas using the process of the present invention (under 100°C) a

vitrified product is produced, which product is a controlled-release product. Thus, this experimental evidence overwhelmingly shows that two different products are produced using the two different methods.

With regard to the Examiner's assertion that the examples in Lentz were not to be construed as limiting, Appellants note that the temperature range of 80°C to 240°C given in the Abstract and on page 13 of Lentz does not mean that the processing takes place at any temperature between 80°C and 240°C. As explained by Dr. Rein in his Declaration at Paragraph 6, one skilled in the art of extrusion would clearly understand that Lentz is giving the range of temperature of the extruder, which temperatures differ at different locations of the extruder. See, for example, page 28, line 18 of Lentz.

With regard to the Examiner finding the evidence provided by Appellants to be not persuasive, Appellants point out that the unsupported opinion of an examiner is insufficient to rebut expert testimony. Cf. *In re Alton*, 76 F.3d 1168 (Fed. Cir. 1996). Pursuant to the Manual of Patent Examining Procedure, § 2145, an examiner "should specifically set forth the facts and reasoning that justifies [his] conclusion." In the present instance, Appellants do not believe that the Examiner has met this requirement. See also, *Ex parte Malone*, 2009 WL 2712145 (Bd. Pat. App. & Interf.).

With regard to the Examiner's statement that Appellants have shown that processing above 100°C results in a foamed product, but that Lentz teaches a range of temperatures below 100°C, Appellants note that when Lentz teaches a temperature under 100°C, the product produced is not a controlled release product (see Figure 10 of Lentz), as required by the claims. Further, and with regard to the Examiner's allegation that the addition of less than 15% by weight water does not limit the amount of water in the final product, Appellants disagree and note that one skilled in the art would understand, in view of the teaching in the specification at page 5, lines 15-17, and page 9, lines 23-25, that the total amount of water by weight percentage in the final product does not exceed 15%. With regard to the Examiner's comment regarding the range in amounts of water used in Lentz in Figure 6, Applicants note that any water content less than 15.8% does not result in controlled release product, thus, demonstrating that the claimed controlled release formulations are different from those described by Lentz.

In view of the foregoing, Appellants submit that this rejection should be reversed and that the claimed methods for producing controlled release matrices and the controlled released matrices set forth in claims 10, 16, 17 and 23-32 are not anticipated by Lentz.

II. The Examiner's Response to Appellants' Arguments That Claims 10, 16-18 and 23-32 Are Not Obvious Is Erroneous

A. With respect to the rejection of claims 10, 16-18 and 23-32 as obvious in view of European Patent Publication No. 0 580 860A1 to Nakamichi *et al.* ("Nakamichi"), Appellants respectfully submit that the response in the Examiner's Answer to Appellants' arguments is erroneous.

As discussed above, Nakamichi does not teach the claimed methods or compositions of the present invention, since Nakamichi does not disclose controlled release compositions or vitrified compositions or methods of making same. The Examiner alleges, however, that it would have been obvious for one skilled in the art to vary the parameters disclosed in Nakamichi to obtain the claimed methods and claimed products.

Appellants respectfully disagree. In order to establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580 (CCPA 1974). In the present case, Nakamichi does not teach or suggest controlled release compositions or methods of making same, as discussed above. Additionally, the Supreme Court, in *KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 82 U.S.P.Q. 1385 (2007), affirmed that "a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art," and that it is "important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does...because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known." *KSR*, S.Ct. at 1741, 82 U.S.P.Q.2d at 1396. In the instant case, Applicants submit that in order to make a *prima facie* case for obviousness, a reason must have been provided to one skilled in the art to vary the parameters in order to achieve the controlled release compositions as claimed. Since no such teaching is provided, Nakamichi cannot render obvious the claimed methods and compositions.

Further, Nakamichi does not teach or suggest which of the many parameters should be adjusted, if any, *e.g.*, temperature, pressure, amount of water, *etc.*, to achieve the desired result. Appellants submit that it would be undue experimentation to try to achieve the claimed invention based on the teachings of Nakamichi since there is no teaching of which of

the parameters were critical and no direction as to which of many possible choices is likely to be successful. At most, the Examiner's rejection is based on an obvious to try standard, which is not the standard of 35 U.S.C. § 103. *Application of Antonie*, 559 F.2d 618 (CCPA 1977), *In re Yates*, 663 F.2d 1054 (CCPA 1981). To have a reasonable expectation of success, one must be motivated to do more than merely vary all parameters or try each of numerous choices until one possibly arrives at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful. *Ex parte Taniguchi*, 2008 WL 3874455 (Bd. Pat. App. & Interf.). Nakamichi does not provide such a teaching or suggestion of the result to be achieved or how to alter its teachings to achieve such result, thus, Nakamichi cannot render obvious the claimed invention.

In view of the foregoing, and Appellants' previously submitted remarks, Appellants submit that this rejection should be reversed and that the claimed method for producing controlled release matrices and the controlled release matrices set forth in claims 10, 16-18 and 23-32 are not rendered obvious by Nakamichi.

B. With respect to the rejection of claims 10, 17-18 and 23-32 as obvious in view of International Patent Publication No. WO 92/15285 to Lentz *et al.* ("Lentz"), Appellants respectfully submit that the response in the Examiner's Answer to Appellants' arguments is erroneous.

As discussed above, the formulations produced by Lentz are different from those as claimed herein. Furthermore, Lentz provides no teaching or suggestion on how to modify its teaching to achieve the claimed methods or controlled release formulations.

With regard to the Examiner's comment that Lentz exemplifies and teaches a range of temperatures below 100°C, and that the processing temperature for the controlled release formulation was 100°C and 70°C, Appellants note that Lentz shows that temperatures under 100°C do not result in the formulation of either a vitrified starch or a controlled release formulation. The results presented in Figure 10 clearly show that processing at 70°C does not result in a controlled release formulation. Comparing the release rate for the 70°C formulation in Figure 10 of Lentz with the lapidus release rate taught in the specification for controlled release (see, *e.g.*, Figure 4/6), one skilled in the art can clearly determine that the 70°C formulation of Lentz is not a controlled release formulation. Thus, in view of this result,

Lentz teaches away from using any processing temperature under 100°C to obtain a controlled release formulation.

Further, Appellants note that the MDS processed starch in Lentz is different from the vitrified processed starch of the present invention, and that Lentz provides no teaching to suggestion to modify the MDS starch to obtain the claimed vitrified starch formulations. Even though both Lentz and the present invention teach destructure of starch by way of extrusion, the nature of the destructured starch obtained is different since the molecularly dispersed starch of Lentz is soft and rubbery and, thus, above glass transition temperature. The extruded matrices obtained by the present invention are vitrified, *i.e.*, rigid and, thus, their temperature never exceeds the glass transition temperature and preferably remains below the glass transition temperature. This structural difference between the starch matrices of the present invention and that of Lentz is a consequence of the differences in the methods taught by Lentz and disclosed in the present specification.

Moreover, experimental evidence comparing the process of the present invention was provided, where the temperature of the extruder orifice is below 100°C, with the process taught by Lentz. The Examiner's attention is invited to the Rein Declaration at Paragraphs 8 to 12 where Dr. Rein sets forth experiments that were performed or supervised and directed by him, and their results demonstrating that using the process of Lentz (over 100°C) only popped (foamed) products are produced, whereas using the process of the present invention (under 100°C) a vitrified product is produced, which product is a controlled-release product. Thus, this experimental evidence overwhelmingly shows that two different products are produced using the two different methods.

With regard to the Examiner's statement that Lentz teaches that the starch can be in several physical forms depending on the processing temperature, Appellants point out that Lentz teaches on page 34, lines 30-32 that the starch, depending on the processing temperature, would have different degrees of destructure, not that the starch would have a completely different physical form, *i.e.*, vitrified, as required by the claims.

A rejection for obviousness is improper when there is nothing in the cited prior art reference suggests the desirability of the claimed subject matter. In the present case, the presently claimed methods are directed to the production of a controlled release matrix by co-extrusion of a dry mixture of a starch and an active agent where the temperature at the orifice of the extruder during the extrusion process is below 100°C under normal pressure. Lentz does not teach or suggest a modification of its disclosed method using destructured starch

(MDS) requiring that the temperature at the orifice of the extruder (as well as all other parts of the extruder) during the extrusion process be below 100°C under normal pressure, to result in a controlled release formulation.

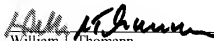
In view of the foregoing, Appellants submit that this rejection should be reversed and that the claimed methods and controlled release matrices set forth in claims 1, 5, 6, 10, 16-18 and 20-32 are not obvious in view of the disclosure of Lentz.

CONCLUSION

For all of the reasons set forth above, Appellants respectfully request that all of the rejections of the claims on appeal be reversed.

Respectfully submitted,

Date: March 11, 2011



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